## REMARKS

Rejection of the claims under 35 USC § 102

Claims 11, 13, 14, 15, and 17 have been rejected under 35 U.S. C. 102(b) as being anticipated by Sioud et al. (Nature Biotech. 1998). The Action states that that the Specification does not define the term vessel. Applicants provide a basis for understanding of the term vessel in the Specification on page 3 lines 19-25. Further, since the term vessel is a common term in the art, the ordinary and customary meaning of the term in the art should apply. While that term vessel can reasonably be interpreted to include veins, arteries, and capillaries (and is so indicated on page 3 lines 19-25), and while vessels may be present in a tumor (or a target tissue), direct injection into a tumor can not be reasonably interpreted, by a person or ordinary skill in the art, to include injection (or insertion) into a vessel. There is no evidence or suggestion in Sioud et al. that Sioud et al. injected or delivered any nucleic acid into a vessel. Nevertheless, Applicants have amended the claims to further distinguish their invention from the teaching of Sioud et al. Specifically, Applicants have amended claim 11 to recite "the rate of injection and the volume of the solution increase permeability of a vessel" and "delivering the double strand RNA oligonucleotide from inside the vessel, through a wall of the vessel, into the extravascular space and into the in vivo parenchymal cell". Support for the rate of injection increasing the permeability of the vessel can be found in the specification on page 3 lines 15-17, page 6 line 5, page 7 lines 19-25, page 7 line 27 to page 8 line 2. Support for the volume of solution increasing the permeability of the vessel can be found in the specification on page 3 lines 15-17, and page 7 lines 2-17. Support for delivering a nucleic acid (double strand RNA oligonucleotide) "from inside the vessel, through a wall of the vessel, into the extravascular space and into the in vivo parenchymal cell" can be found in the specification on page 3 lines 14-15, page 3 lines 24-25, and page 5 line 25 to page 6 line 2. Support for delivery to an in vivo parenchymal cell is found throughout the specification.

Claims 11, 13, 14, and 17 have been rejected under 35 U.S. C. 102(b) as being anticipated by Czubayko et al. (PNAS 1996). Applicants respectfully disagree. The Action states that the term comprising does not exclude the transfection of a ribozymes into a cell in vitro and insertion of

the cells into a mouse. Czubayko et al. teaches injection into a flank, not a vessel. Czubayko et al. fails to teach delivery of any nucleic acid to any parenchymal cell in a mammal. Czubayko et al. fails to teach increasing permeability of a vessel. Nevertheless, it is the Applicants' opinion that the amendments described above further distinguish the Applicants' process from that taught by Czubayko et al. and are sufficient to obviate the rejection.

Rejection of the claims under 35 USC § 103

Claims 11 and 13-18 have been rejected under 35 U.S. C. 103 as being unpatentable over Zimmer (Methods, 1999) in view of Vaish et al (NAR 1998) and Zhang et al (Human Gene Therapy 1999). It is the Applicants' opinion that the amendments to the claims, described above, are sufficient to obviate the rejection. In light of the amendments, Applicants request reconsideration of the §103 rejection.

The Examiner's objections and rejections are now believed to be overcome by this response to the Office Action. In view of Applicants' amendment and arguments, it is submitted that claims 11 and 13-18 should be allowable.

Respectfully submitted,

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I hereby certify that this correspondence is being transmitted to the USPTO on this date: April 12, 2007 .

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